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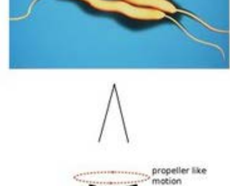
LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN GRK2062

WHAT'S GOING ON

in the Research Training Group Molecular Principles of Synthetic Biology

NEWSLETTER #4 2016

FOCUS ON RESEARCH



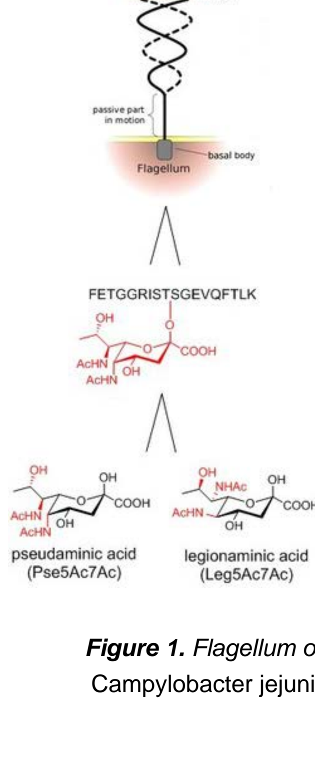


Figure 1. *Flagellum of* Campylobacter jejuni.

Prof. Dr. Anja Hoffmann-Röder

Glycosylation

Glycosylation, i.e., the attachment of sugar residues to protein side-chains, is the most prevalent of all known post-translational modifications. It has been estimated that more than half of the proteins in nature are glycoproteins. The role of these glycan structures for biological function, however, has long been underestimated by the scientific community. This view has changed completely and it is now well-recognized that carbohydrates play key roles in health and disease by participating in multiple biological processes including immunity, fertilization, cellular communication, and cell differentiation. The huge structural diversity of naturally occurring glycans builds the molecular basis for diverse biological roles, but at the same time hampers elucidation of structure-function relationships. To date, controlling glycosylation to a well-defined glycoform during protein expression is still very challenging, and current chromatographic techniques are unable to isolate different glycoprotein glycoforms on a practical scale. On the other hand, chemical synthesis holds enormous promise by providing structurally well-defined homogeneous glycans for functional studies. Moreover, it allows access to designed synthetic analogs with improved molecular properties for biological research and biomedical applications.

In my group, we study the chemical synthesis of flagellin A glycopeptides from of the human pathogen *Campylobacter jejuni*, which is the most frequent causative agent of bacterial gastroenteritis worldwide. Although preliminary studies on recombinant proteins have demonstrated the importance of accurate glycosylation, precise structure-activity relationships with regard to the sites and structure of the glycans (i.e., minimal functional glycan composition), as well as their preferred binding partners are not known. Moreover, we will use our synthetic glycopeptides for the construction of diagnostic devices and for the development of highly specific anti-bacterial vaccines.

GRK2062 PUBLICATION

Nucleic Acids Research, July 12th 2016

The target spectrum of SdsR small RNA in *Salmonella*

Kathrin S. Fröhlich, Katharina Haneke, Kai Papenfort and Jörg Vogel

Abstract

Model enteric bacteria such as *Escherichia coli* and *Salmonella enterica* express hundreds of small non-coding RNAs (sRNAs), targets for most of which are yet unknown. Some sRNAs are remarkably well conserved, indicating that they serve cellular functions that go beyond the necessities of a single species. One of these 'core sRNAs' of largely unknown function is the abundant ~100-nucleotide SdsR sRNA which is transcribed by the general stress σ-factor, σ^S and accumulates in stationary phase. In *Salmonella*, SdsR was known to inhibit the synthesis of the species-specific porin, OmpD. However, *sdsR* genes are present in almost all enterobacterial genomes, suggesting that additional, conserved targets of this sRNA must exist. Here, we have combined SdsR pulse-expression with whole genome transcriptomics to discover 20 previously unknown candidate targets of SdsR which include mRNAs coding for physiologically important regulators such as the carbon utilization regulator, CRP, the nucleoid-associated chaperone, StpA and the antibiotic resistance transporter, TolC. Processing of SdsR by RNase E results in two cellular SdsR variants with distinct target spectra. While the overall physiological role of this orphan core sRNA remains to be fully understood, the new SdsR targets present valuable leads to determine sRNA functions in resting bacteria.

http://dx.doi.org/10.1093/nar/gkw632

NEW MEMBERS

PhD-students

Christopher Scheidler, M.Sc. Biochemistry, started his PhD study in February 2016. Supervised by Sabine Schneider he is focusing on "Development of a genetic code expansion system in *Bacillus subtilis*".

EVENTS

Photo: *The iGEM team 2016 presented information about their project during the Open House of the LMU Biocenter on July 14, 2016.*

Report iGEM Team 2016

3D printing has become a revolutionary technology in various industries, including biotechnology. A particularly attractive application currently emerges in the area of synthetic biology, in the context of regenerative tissue and organ engineering. Apart from therapy, 3D printing could also aid in the supply of biosynthetic skin or miniature organs for use in the testing of cosmetics or drugs, respectively.

Therefore, a team of fourteen students embraced this concept and endeavoured to develop an innovative 3D tissue printing approach under the patronage of GRK2062 and supported by both Munich universities. With this ambitious project we participate in this year's iGEM competition, an international contest focused at synthetic biology and bringing together more than 300 university teams worldwide. We look forward to presenting our results at the final "jamboree" hosted by the MIT (Cambridge, USA) this October.

Our project incorporates aspects of three major scientific disciplines: biotechnology, engineering, and medicine. Our BioPrinting approach relies on one of the strongest known non-covalent molecular interactions: the tight complex formation between the protein streptavidin and biotin (Vitamin H). Using appropriately designed biomolecular components, this extraordinary affinity enables the construction of a stable three-dimensional network.

Thus, our "BioInk" consists of two components: (i) live ***cells*** with biotin anchored to surface proteins mixed with (ii) a biotinylated fibrillar ***linker protein***, for example collagen. While this ink cannot self-aggregate, crosslinking will immediately occur once it is printed into the liquid matrix, that is a reservoir solution containing a high concentration of the tetravalent biotin-binding protein ***streptavidin***. This allows the generation of individual shaped three-dimensional cellular arrays at will. To equip our cells with *in vivo* biotinylated surface proteins, we will generate a modified cell surface receptor based on the EGFR transmembrane and extracellular domains that carries the substrate peptide sequence of biotin ligase.

The modularity of this approach greatly simplifies adaption to prescribed tasks and aspired physical properties, e.g. by varying the length or structure of the linker protein or the density of the biotin groups. Furthermore, the cells may be omitted, in order to print a protein scaffold first, for subsequent population with suitable target cells. This renders our strategy even more versatile than the conventional use of collagen matrices.

Apart from these biotechnological aspects, we implement engineering science into our project by adapting a commercial 3D plastic printer to the task of printing the bioink/cells. Eventually, we plan to enable our biosynthetic 3D-printed tissue to produce/secrete therapeutically relevant proteins, e.g. insulin.

We will be happy to report on our progress in subsequent issues of this Newsletter. Also, we are grateful to GRK2062 and Professor Skerra for supporting us to participate in this year's iGEM competition.

Upcoming Transferable Skills Courses

Adobe Illustrator

Andreas Binder will hold this course on the 13th and 14th of October 2016 in room G00.037 at LMU Biocenter. The workshop will cover both basic and more advanced functions of the software, which will be helpful to generate scientific posters, figures and presentations (more details). For registration please send an e-mail to grk2062@bio.lmu.de.

JOURNAL CLUB

Science 352 (6287), 833-836

Report

A high-yielding, strictly regioselective prebiotic purine nucleoside formation pathway

Sidney Becker, Ines Thoma, Amrei Deutsch, Tim Gehrke, Peter Mayer, Hendrik Zipse, Thomas Carell

Abstract

The origin of life is believed to have started with prebiotic molecules reacting along unidentified pathways to produce key molecules such as nucleosides. To date, a single prebiotic pathway to purine nucleosides had been proposed. It is considered to be inefficient due to missing regioselectivity and low yields.We report that the condensation of formamidopyrimidines (FaPys) with sugars provides the natural *N*-9 nucleosides with extreme regioselectivity and in good yields (60%). The FaPys are available from formic acid and aminopyrimidines, which are in turn available from prebiotic molecules that were also detected during the Rosetta comet mission. This nucleoside formation pathway can be fused to sugar-forming reactions to produce pentosides, providing a plausible scenario of how purine nucleosides may have formed under prebiotic conditions.

Full text: http://dx.doi.org/10.1126/science.aad2808

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MOLECULAR PRINCIPLES OF SYNTHETIC BIOLOGY

LMU

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